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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,335	CEVC ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-79* is/are pending in the application.

4a) Of the above claim(s) *46,49,51-54,56,57,61 and 68-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-45,47,48,50,55,58-60 and 62-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/30/03; 1/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed 3/14/2006 is acknowledged. Claims 1-36 have been cancelled. New claims 37-79 are pending. Claims 46, 49, 51-54, 56-57, 61, and 68-79 have been withdrawn as being drawn to nonelected inventions. Claims 37-45, 47-48, 50, 55, 58-60, and 62-67 are currently under examination.

Information Disclosure Statement

The information disclosure statements filed 12/30/2003 and 1/30/2004 have been considered. Initialed copies are enclosed.

Election/Restrictions

Applicant's election with traverse of Group I in the response filed 3/14/2006 is acknowledged. The traversal is on the ground(s) that Paul *et al.*, cited in the restriction requirement of 9/15/2006, does not anticipate the instantly claimed invention, and thus there is a special technical feature linking the groups of inventions. Applicant argues that the composition disclosed by Paul *et al.* is not a vaccine because the reference does not disclose that the composition provides protective immunity. This is not found persuasive because the ability to induce a protective immune response is an inherent property of a given antigen. Moreover,Paul *et al.* disclose that the transdermal antigen delivery composition is intended for use as a vaccine (see page 146, paragraph 3). Further, the term "vaccine" is an intended use and is given no patentable weight, therefore the claims are interpreted as a composition. The composition disclosed by Paul *et al.* meets all of the limitations found in claim 1 of the instant application. Therefore, there is no special technical feature linking the groups in the instant application.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

Claims 37-45, 47-48, 50, 55, 58-60, and 62-67 are objected to because of the following informalities: The claims are drawn, in part, to non-elected inventions. Appropriate correction is required.

Claim 58 is objected to because of the following informalities: The claims recites the phrase "wherein the low molecular weight irritant from the group of surfactant-like molecules." It appears that a typographical error has been made and the claim should state "selected from the group." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-45, 47-48, 50, 55, 58-60, and 62-67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a transdermal vaccine that comprises a transdermal carrier, a compound which specifically has or induces cytokine or anti-cytokine activity, and an antigen derived from pathogens triggering tetanus. The claims encompass all antigens that can be derived from pathogens triggering tetanus, including proteins, cell wall constituents, and the tetanus toxin of *Clostridium tetani*. To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that applicant has possession the claimed invention. To adequately describe the genus of antigens derived from pathogens triggering tetanus, applicant must adequately describe the antigenic determinants (immunoepitopes) that elicit a protective immune response when administered transdermally.

The specification, however, does not disclose distinguishing and identifying features of a representative number of members of the genus of antigens to which the claims are drawn, such as a correlation between the structure of the immunoepitope and its recited function (to elicit a protective immune response against pathogens triggering tetanus), so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of antigens. Moreover, the specification fails to disclose which amino acid residues are essential to the function of the immunoepitope or which amino acids might be replaced so that the resultant immunoepitope retains the activity of its parent, or by which other amino acids the essential amino acids might be replaced so that the resultant immunoepitope retains the activity of its parent. Therefore, since the specification fails to adequately describe at least a substantial number of members of the genus of immunoepitopes to which the claims are based; the specification fails to adequately describe at least a substantial number of members of the claimed genus of antigens that can be derived from pathogens triggering tetanus.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to

practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. As evidenced by Greenspan et al. (*Nature Biotechnology* 7: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a protective immune response to a given pathogen can only be identified empirically. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of immunoepitopes, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antigens that can be derived from pathogens triggering tetanus. Therefore, because the art is unpredictable, in

accordance with the *Guidelines*, the description of immunoepitopes (antigenic determinants) is not deemed representative of the genus of antigens to which the claims refer. Hence, only a vaccine containing tetanus toxoid meets the written description requirements.

Claims 37-45, 47-48, 50, 55, 58-60, and 62-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for vaccines comprising tetanus toxoid as the antigen, does not reasonably provide enablement for vaccines comprising an antigen derived from pathogens triggering tetanus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The instant claims are drawn to a transdermal vaccine that comprises a transdermal carrier, a compound which specifically has or induces cytokine or anti-

cytokine activity, and an antigen derived from pathogens triggering tetanus. The claim encompasses all antigens that can be found in, and are expressed by, a *Clostridium tetani* cell, including proteins, cell wall constituents, and the tetanus toxin.

Guidance of the specification/The existence of working examples: The specification discloses, in the examples, challenge experiments using the claimed vaccine wherein the antigen is tetanus toxoid. The specification is devoid of any teaching that any antigen other than the tetanus toxoid provides an effective vaccine against any disease, when administered transdermally. To be a prophylactic composition, the composition must elicit protective immunity, demonstrable by pathogen challenge experiments in a reasonable model system. The skilled artisan would clearly realize the critical deficiency of this specification with respect to vaccines. There is absolutely no demonstration of protective immunity upon the transdermal administration in any animal model of disease by all of the antigens encompassed by the claims. Therefore it is not clear which of the claimed antigens are capable of generating a protective immune response against a given disease, when administered transdermally.

State of the art: Although many investigators have tried to develop vaccines based on specific antigens, it is well understood that the ability of an antigen to stimulate antibody production does not necessarily correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from infection (Chandrashekar *et al.*, US Patent 6,248,329, col. 1, lines 35-41). It is well recognized in the vaccine art, that it is unclear whether an antigen derived from a pathogen will elicit protective immunity. Ellis (Chapter 29 of Vaccines, Plistkin, *et al.* (eds) WB Saunders, Philadelphia, 1998, especially p. 571, paragraph 2) exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies... and thus protect the host against attack by the pathogen."

The specification fails to teach that any of the claimed antigens other than the tetanus toxoid can produce a protective response in the host, as is requisite of a vaccine composition. In view of the lack of support in the art and specification for an effective vaccine comprising the claimed proteins, it would require undue experimentation on the part of the skilled artisan to make and use the vaccine as claimed; therefore the full scope of the claims are not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37-45, 47-48, 50, 55, 58-60, and 62-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 is rendered vague and indefinite by the phrase "the penetrant in the form of a minute fluid droplet surrounded by a coating of one or more layers of at least 2 substances that differ by at least a factor of 10 in solubility in a liquid medium." First, it is unclear how one can have one layer of 2 substances. Second, it is unclear how a substance could have any amount of solubility in something other than a liquid medium, as the term "solubility" refers to a substances ability to dissolve in a liquid. Third, is the "penetrant" the fluid droplet itself, or is it the aggregate of the fluid droplet surrounded by the coating. Fourth, if the antigen or allergen is not actually found in the penetrant, it would not penetrate the skin, and would therefore be unable to cause an immune response.

Claim 37 is rendered vague and indefinite by the phrase "an antigen or mixture thereof." To what mixture of antigens is applicant referring? Does the vaccine contain a single antigen or mixtures of antigen?

Claim 38 is rendered vague and indefinite by the phrase "wherein the at least two substances are two different forms of a substance." It is not clear how two substances can be one substance, even in two forms. Are there two substances or are there two forms of one substance?

Claim 39 is rendered vague and indefinite by the phrase "the antigen or allergen are associated with the penetrant." It is not clear what the term "associated" is intended to mean. According to the parent claim, the antigen or allergen and penetrant are already in a vaccine composition, and are thus associated. Does applicant intend that there be some other form of association?

Claims 40, 58-59 are rendered vague and indefinite by the phrase "surfactant-like molecule." What is a surfactant-like molecule? Is it a surfactant, or not? What properties must said molecule have in order to be "surfactant-like"?

Claim 42 is rendered vague and indefinite by the phrase "wherein the total weight of droplets in the vaccine for use on human or animal skin is 0.01 weight-% (w-%) to 40 w-% of total mass." The weight of the droplets should be 0.01-40w-% of the total mass of what? Is applicant referring to the total mass of the human or animal, human or animal skin, penetrant mass, or of the vaccine?

Claim 47 is rendered vague and indefinite by the phrase "derived from." It is unclear what the term "derived from" is intended to mean.

Claim 48 is rendered vague and indefinite by the phrase "pathogens triggering tetanus." It is unclear to what pathogens, other than *Clostridium tetani*, applicant is referring, as *Clostridium tetani* is regarded within the art as the etiological agent of tetanus.

Claim 50 is rendered vague and indefinite by the phrase "wherein the concentration of each compound used." To what compounds is applicant referring? Does applicant mean the compound which specifically has or induces cytokine or anti-cytokine activity, or does applicant mean each of the compounds used to make up the vaccine?

The term " low molecular weight irritant " in claims 44, 58, and 60 is a relative term which renders the claim indefinite. The term "low" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 65 is rendered vague and indefinite by the phrase "pure or purified antigen." It is unclear what limitations are engendered by the term "pure or purified." Purified and pure are relative terms. To what degree are the antigens to be purified? How are said antigens to be purified? As the claim is drawn using open language (comprising), the composition can contain molecules in addition to the antigen. Is a purified antigen mixed with a contaminant still pure?

Claim 67 is rendered vague and indefinite by the phrase "at least one injectable dose of an antigen." It is unclear what an "injectable dose" is. Virtually any liquid can be injected. Are there limitations applicant intends by the term "injectable dose"?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 37, 39-45, 47-48, 50, 55, 58-60, and 62-67 rejected under 35 U.S.C. 103(a) as being unpatentable over Glenn *et al.* (PCT Publication, WO 98/20734, 1998) in view of Paul *et al.* (Vaccine Res., 4:145-164, 1995, IDS filed 12/30/2003).

The instant claims are drawn to a transdermal vaccine, comprising: (a) a transdermal carrier comprising a penetrant suspended or dispersed in an aqueous solvent, the penetrant in the form of a minute fluid droplet surrounded by a coating of one or more layers of at least 2 substances that differ by at least a factor of 10 in solubility in a liquid medium, the substances forming homoaggregates of one substance and/or heteroaggregates of the at least 2 substances, the average diameter of homoaggregates of the more soluble substance, or the average diameter of the heteroaggregates of the at least 2 substances, being smaller than the average diameter of homoaggregates of the less soluble substance, and/or the more soluble substance solubilizing the droplet and the content of the more soluble substance being up to 99 mol-% of the concentration required to solubilize the droplet or corresponding to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or wherein the elastic deformation energy of the droplet surrounded by the coating is at least 5 times lower than the

elastic deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains; (b) a compound which specifically has or induces cytokine or anti- cytokine activity; and (c) an antigen or mixture thereof and/or an allergen or mixture thereof. Further limitations to the vaccine include: the vaccine wherein the compound and the antigen or allergen are associated with the penetrant (claim 39); wherein the less soluble substance with the tendency to aggregate is a polar lipid, and the more soluble substance is a surfactant or a surfactant-like molecule (claim 40); wherein the penetrant is between 30 nm and 500 nm (claim 41); wherein the total weight of droplets in the vaccine for use on human or animal skin is 0.01 weight-% to 40 w-% of total mass (claim 42); wherein total antigen concentration is between 0.001 and 40 w-% of the total penetrant mass (claim 43); comprising a low molecular weight chemical irritant (claim 44); wherein the compound is IL-12 (claim 45); wherein the antigen is derived from pathogens triggering tetanus (claims 47-48); wherein the concentration of each compound used is up to 1000 times higher than a concentration optimum established in corresponding tests performed by injecting the vaccine or performing the tests *in vitro* (claim 50); wherein the concentration of the compound from a pathogen is between 10 times lower and up to 1000 times higher than the concentration used with the corresponding injected vaccines employing similar antigen (claim 55); wherein the low molecular weight irritant is a surfactant-like molecule (claim 58); wherein the surfactant-like molecule enhances skin permeation (claim 59); wherein the concentration of the low molecular weight irritant is below by at least a factor of 2 to a factor of 10 or more a concentration which is unacceptable owing to local irritation in tests on the same or a comparable subject (claim 60); wherein the applied dose of the antigen differs by the factor of 0.1 to 100 from the dose which would have to be used with an injection (claim 62); wherein the applied dose of an antigen is less than 10 times higher than the dose which would have to be used with an injection (claim 63); wherein the applied penetrant dose is between 0.1 mg/cm^2 and 15 mg/cm^2 (claim 64); and wherein the antigen is a pure of purified antigen (claim 65). Further claims are drawn to a kit containing the vaccine of claim 37 in a packaged form (claim 66) and said kit comprising an injectable dose of an antigen (claim 67).

Glenn *et al.* disclose a transdermal vaccine that contains tetanus toxoid and interleukin-12 (see abstract; page 16, lines 15-17; and page 18, lines 15-30). Glenn *et al.* state that the antigens used in the vaccine can be purified (see paragraph bridging pages 15-16).

Glenn *et al.* differs from the instant invention in that the transdermal vaccine does not comprise a carrier wherein the substances forming homoaggregates of one substance and/or heteroaggregates of the at least 2 substances, the average diameter of homoaggregates of the more soluble substance, or the average diameter of the heteroaggregates of the at least 2 substances, being smaller than the average diameter of homoaggregates of the less soluble substance, and/or the more soluble substance solubilizing the droplet and the content of the more soluble substance being up to 99 mol-% of the concentration required to solubilize the droplet or corresponding to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or wherein the elastic deformation energy of the droplet surrounded by the coating is at least 5 times lower than the elastic deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains.

Paul *et al.* disclose an transdermal vaccine (see page 146, paragraph 3) that comprises a transdermal carrier known as a transfersome that comprises ethanolic soybean phosphatidylcholine, sodium cholate, and an antigen (see page 148, Transfersomes preparation). Said transfersomes have the same composition as the claimed vaccine carrier and would thus necessarily have the same physical and immunological properties as the claimed vaccine transfersomes. Additionally, Paul *et al.* disclose that transdermal immunization using large protein molecules can be accomplished using said transfersomes, and that, if properly optimized, a transdermal drug transfer efficacy of > 90% can be achieved (see page 162, paragrahs 7-8). Paul *et al.* further disclose that vaccination can be accomplished using full size proteins across the intact skin (see page 146, paragraph 3).

It would have been obvious to one of ordinary skill in the art to use the transdermal carrier (transfersomes) of Paul *et al.* in the vaccine of Glenn *et al.* in order to take advantage of the high drug transfer efficacy of transfersomes, as disclosed by Paul *et al.* One would have had a reasonable expectation of success because Paul *et al.* disclose that their transfersomes are capable of delivering full size proteins across the skin in a vaccination. Regarding claim 40, phosphatidylcholine is a polar lipid and sodium cholate is a surfactant. Regarding claims 44 and 58, the low molecular weight is claimed as a surfactant-like molecule. Sodium cholate is a surfactant, and is thus surfactant-like. Regarding claims 41-43, 50, 55, 60, and 62-64, these claims are merely optimized ranges for materials in the vaccine. Paul *et al.* disclose that the

vaccine should be properly optimized to achieve efficacy. Further, according to MPEP 2144.05, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Regarding claims 66 and 67, the vaccine disclosed by the prior art are packaged in some form, thus anticipating the limitation of a kit containing said vaccine in a packaged form. The vaccine taught by the combination of Paul *et al.* and Glenn *et al.* would be injectable. Therefore, as the vaccine disclosed by the prior art contains a dose of antigen, the prior art anticipates this limitation.

Conclusion

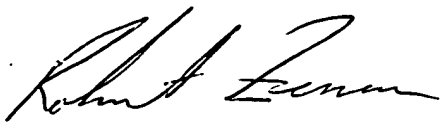
No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Gangle whose telephone number is 571-272-1181. The examiner can normally be reached on M-F 8:00 am - 4:30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Brian Gangle
AU 1645



ROBERT ZEMAN
PATENT EXAMINER